

Connecting via Winsock to STN

Welcome to STN International! Enter x:x

LOGINID:SSPTANXR1625

PASSWORD:

TERMINAL (ENTER 1, 2, 3, OR ?):2

\* \* \* \* \* Welcome to STN International \* \* \* \* \*

NEWS	1		Web Page for STN Seminar Schedule - N. America
NEWS	2	JUL 02	LMEDLINE coverage updated
NEWS	3	JUL 02	SCISEARCH enhanced with complete author names
NEWS	4	JUL 02	CHEMCATS accession numbers revised
NEWS	5	JUL 02	CA/Capplus enhanced with utility model patents from China
NEWS	6	JUL 16	CAplus enhanced with French and German abstracts
NEWS	7	JUL 18	CA/Capplus patent coverage enhanced
NEWS	8	JUL 26	USPATFULL/USPAT2 enhanced with IPC reclassification
NEWS	9	JUL 30	USGENE now available on STN
NEWS	10	AUG 06	CAS REGISTRY enhanced with new experimental property tags
NEWS	11	AUG 06	FSTA enhanced with new thesaurus edition
NEWS	12	AUG 13	CA/Capplus enhanced with additional kind codes for granted patents
NEWS	13	AUG 20	CA/Capplus enhanced with CAS indexing in pre-1907 records
NEWS	14	AUG 27	Full-text patent databases enhanced with predefined patent family display formats from INPADOCDB
NEWS	15	AUG 27	USPATOLD now available on STN
NEWS	16	AUG 28	CAS REGISTRY enhanced with additional experimental spectral property data
NEWS	17	SEP 07	STN AnaVist, Version 2.0, now available with Derwent World Patents Index
NEWS	18	SEP 13	FORIS renamed to SOFIS
NEWS	19	SEP 13	INPADOCDB enhanced with monthly SDI frequency
NEWS	20	SEP 17	CA/Capplus enhanced with printed CA page images from 1967-1998
NEWS	21	SEP 17	CAplus coverage extended to include traditional medicine patents
NEWS	22	SEP 24	EMBASE, EMBAL, and LEMBASE reloaded with enhancements
NEWS	23	OCT 02	CA/Capplus enhanced with pre-1907 records from Chemisches Zentralblatt
NEWS	24	OCT 19	BEILSTEIN updated with new compounds
NEWS	25	NOV 15	Derwent Indian patent publication number format enhanced
NEWS	26	NOV 19	WPIX enhanced with XML display format
NEWS	27	NOV 30	ICSD reloaded with enhancements
NEWS	28	DEC 04	LINPADOCDB now available on STN

NEWS EXPRESS 19 SEPTEMBER 2007: CURRENT WINDOWS VERSION IS V8.2,  
CURRENT MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP),  
AND CURRENT DISCOVER FILE IS DATED 19 SEPTEMBER 2007.

NEWS HOURS	STN Operating Hours Plus Help Desk Availability
NEWS LOGIN	Welcome Banner and News Items
NEWS IPC8	For general information regarding STN implementation of IPC 8

Enter NEWS followed by the item number or name to see news on that specific topic.

All use of STN is subject to the provisions of the STN Customer agreement. Please note that this agreement limits use to scientific

research. Use for software development or design or implementation of commercial gateways or other similar uses is prohibited and may result in loss of user privileges and other penalties.

\* \* \* \* \* STN Columbus \* \* \* \* \*

FILE 'HOME' ENTERED AT 11:33:18 ON 07 DEC 2007

=> file caplus

COST IN U.S. DOLLARS

SINCE FILE

TOTAL

ENTRY

SESSION

FULL ESTIMATED COST

0.21

0.21

FILE 'CAPLUS' ENTERED AT 11:33:35 ON 07 DEC 2007

USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.

PLEASE SEE "HELP USAGETERMS" FOR DETAILS.

COPYRIGHT (C) 2007 AMERICAN CHEMICAL SOCIETY (ACS)

Copyright of the articles to which records in this database refer is held by the publishers listed in the PUBLISHER (PB) field (available for records published or updated in Chemical Abstracts after December 26, 1996), unless otherwise indicated in the original publications. The CA Lexicon is the copyrighted intellectual property of the American Chemical Society and is provided to assist you in searching databases on STN. Any dissemination, distribution, copying, or storing of this information, without the prior written consent of CAS, is strictly prohibited.

FILE COVERS 1907 - 7 Dec 2007 VOL 147 ISS 25

FILE LAST UPDATED: 6 Dec 2007 (20071206/ED)

Effective October 17, 2005, revised CAS Information Use Policies apply. They are available for your review at:

<http://www.cas.org/infopolicy.html>

=> s PDE activity

5611 PDE

1080 PDES

6054 PDE

(PDE OR PDES)

2285827 ACTIVITY

455568 ACTIVITIES

2477934 ACTIVITY

(ACTIVITY OR ACTIVITIES)

L1 914 PDE ACTIVITY

(PDE(W)ACTIVITY)

=> s l1 and FP assay?

9045 FP

1278 FPS

10116 FP

(FP OR FPS)

579837 ASSAY?

75 FP ASSAY?

(FP(W)ASSAY?)

L2 0 L1 AND FP ASSAY?

=> s FP assay?

9045 FP

1278 FPS

10116 FP

(FP OR FPS)

579837 ASSAY?

L3            75 FP ASSAY?  
              (FP(W)ASSAY?)

=> s l3 and inflammatory?  
      192527 INFLAMMATORY?

L4            1 L3 AND INFLAMMATORY?

=> d ibib abs hitstr tot

ACCESSION NUMBER: 2007.1090909 CAPLUS  
DOCUMENT NUMBER: 147:406707  
TITLE: Preparation of quinoline derivatives as PDE4 inhibitors  
INVENTOR(S): Edlin, Christopher David; Holman, Stuart  
PATENT ASSIGNEE(S): Glaxo Group Limited, UK  
SOURCE: PCT Int. Appl., 38pp.  
CODEN: PIXXD2  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
FAMILY ACC. NUM. COUNT: 1  
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2007107499	A1	20070927	WO 2007-EP52478	20070315
M: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, MT, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
PRIORITY APPLN. INFO.:		GB 2006-5462	A 20060317	
OTHER SOURCE(S):		MARPAT 147:406707		
GI				

\* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT \*

AB The title compds. with general formula I [wherein R1 = alkyl or cycloalkyl; R2 = halo or CN] or pharmaceutically acceptable salts or solvates thereof were prepared as inhibitors of phosphodiesterases (PDEs) for the treatment or prophylaxis of diseases for which a PDE4 inhibitor

is indicated, in particular, inflammatory or allergic diseases such as chronic obstructive pulmonary disease (COPD), asthma, rheumatoid arthritis, or allergic rhinitis. For example,

4-[(3-chlorophenylamino)-8-methyl-6-(4-piperidinylsulfonyl)-3-quinolinecarboxamide dihydrochloride (preparation given) was reacted with iso-Pr sulfonyl chloride in presence of

N,N-diisopropylethylamine in N,N-dimethylformamide to give II as a final product. I showed PDE4 inhibitory activity with IC50 values of >9.5 in fluorescence polarisation (FP) assays.

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE  
FORMAT

=> s l3 and allerg?

75412 ALLERG?

L5 1 L3 AND ALLERG?

=> d ibib abs hitstr tot

15 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2007 ACS on STM

ACCESSION NUMBER: 2007:1080909 CAPLUS  
DOCUMENT NUMBER: 147:406707  
TITLE: Preparation of quinoline derivatives as PDE4 inhibitors  
INVENTOR(S): Edlin, Christopher David; Holman, Stuart  
PATENT ASSIGNEE(S): Glaxo Group Limited, UK  
SOURCE: PCT Int. Appl., 38pp.  
CODEN: PIXXD2  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
FAMILY ACC. NUM. COUNT: 1  
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2007107499	A1	20070927	WO 2007-EP52478	20070315
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, MT, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GO, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
PRIORITY APPLN. INFO.:		GB 2006-5462	A 20060317	
OTHER SOURCE(S):		MARPAT 147:406707		
GI				

\* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT \*

AB The title compds. with general formula I [wherein R1 = alkyl or cycloalkyl; R2 = halo or CN] or pharmaceutically acceptable salts or solvates thereof were prepared as inhibitors of phosphodiesterases (PDEs) for the treatment or prophylaxis of diseases for which a PDE4 inhibitor

is indicated, in particular, inflammatory or allergic diseases such as chronic obstructive pulmonary disease (COPD), asthma, rheumatoid arthritis, or allergic rhinitis. For example, 4-[(3-chlorophenylamino)-8-methyl-6-(4-piperidinylsulfonyl)-3-quinolinecarboxamide dihydrochloride (preparation given) was reacted with iso-Pr sulfonyl chloride in presence of N,N-diisopropylethylamine in N,N-dimethylformamide to give II as a final product. I showed PDE4 inhibitory activity with IC50 values of >9.5 in fluorescence polarization (FP) assays.

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE

FORMAT

=> s l1 and inflammatory?  
192527 INFLAMMATORY?  
L6 40 L1 AND INFLAMMATORY?

=> s l6 and allerg?  
75412 ALLERG?  
L7 9 L6 AND ALLERG?

=> d ibib abs hitstr tot

L7 ANSWER 1 OF 9 CAPLUS COPYRIGHT 2007 ACS ON STN  
 ACCESSION NUMBER: 2006:1105075 CAPLUS  
 DOCUMENT NUMBER: 146:19897  
 TITLE: Inhibition of phosphodiesterase activity, airway inflammation and hyperresponsiveness by PDE4 inhibitor  
 and glucocorticoid in a murine model of allergic asthma  
 AUTHOR(S): Sun, Jian-gang; Deng, Yang-mei; Wu, Ximei; Tang, Hui-fang; Deng, Jun-fang; Chen, Ji-qiang; Yang, Shui-you; Xie, Qiang-min  
 CORPORATE SOURCE: Zhejiang Respiratory Drugs Research Laboratory of State Food and Drug Administration, Medical Science College of Zhejiang University, Hangzhou, 310031, Peop. Rep. China  
 SOURCE: Life Sciences (2006), 79(22), 2077-2085  
 CODEN: LIFSAK; ISSN: 0024-3205  
 PUBLISHER: Elsevier B.V.  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English  
 AB Phosphodiesterase 4 (PDE4) isoenzyme plays important roles in inflammatory and immunomodulatory cells. In this study, piclamilast, a selective PDE4 inhibitor, was used to investigate the role of PDE4 in respiratory function and inflammation in a murine asthma model.  
 Sensitized mice were challenged with aerosolized ovalbumin for 7 days, piclamilast (1, 3 and 10 mg/kg) and dexamethasone (2 mg/kg) were orally administered once daily during the period of challenge. Twenty-four hours after the last challenge, airway hyperresponsiveness to methacholine was determined by whole-body plethysmog., airway inflammation and mucus secretion by histomorphometry, pulmonary cAMP-PDE activity by HPLC, cytokine levels in bronchoalveolar lavage fluid and their mRNA expression in lung by ELISA and RT-PCR, resp. In control mice, significant induction of cAMP-PDE activity was parallel to the increases of hyperresponsiveness, inflammatory cells, cytokine levels, mRNA expression as well as goblet cell hyperplasia. However, piclamilast dose-dependently and significantly improved airway resistance and dynamic compliance, and the maximal effect was similar to that of dexamethasone. Piclamilast treatment dose-dependently and significantly prevented the increase in inflammatory cell number and goblet cell hyperplasia, as well as production of cytokines, including eotaxin, TNF $\alpha$  and IL-4. Piclamilast exerted a weaker inhibitory effect than dexamethasone on eosinophils and neutrophils, had no effect on lymphocyte accumulation. Moreover, piclamilast inhibited up-regulation of cAMP-PDE activity and cytokine mRNA expression; the maximal inhibition of cAMP-PDE was greater than that exerted by dexamethasone, and was similar to dexamethasone on cytokine mRNA expression. This study suggests that inhibition of PDE4 by piclamilast robustly improves the pulmonary function, airway inflammation and goblet cell hyperplasia in murine allergenic asthma.  
 REFERENCE COUNT: 34 THERE ARE 34 CITED REFERENCES AVAILABLE FOR THIS  
 RECORD. ALL CITATIONS AVAILABLE IN THE RE  
 FORMAT

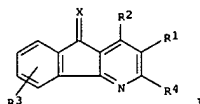
L7 ANSWER 3 OF 9 CAPLUS COPYRIGHT 2007 ACS ON STN  
 ACCESSION NUMBER: 2006:521711 CAPLUS  
 DOCUMENT NUMBER: 144:487025  
 TITLE: The role of PDE4 in pulmonary inflammation and goblet cell hyperplasia in allergic rats  
 AUTHOR(S): Tang, Hui-Fang; Chen, Ji-Qiang; Xie, Qiang-Min; Zheng, Xu-Yang; Zhu, Yi-Liang; Adcock, Ian; Wang, Xiangdong  
 CORPORATE SOURCE: Zhejiang Respiratory Drugs Research Laboratory of State Foods and Drugs Administration of China,  
 Medical School of Zhejiang University, Hangzhou, 310031,  
 Peop. Rep. China  
 SOURCE: Biochimica et Biophysica Acta, Molecular Basis of Disease (2006), 1762(5), 525-532  
 CODEN: BBADEX; ISSN: 0925-4439  
 PUBLISHER: Elsevier B.V.  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English  
 AB Phosphodiesterase 4 (PDE4) has been suggested to a critical factor in the pathogenesis of inflammation by metabolizing cAMP in human leukocytes, endothelium and epithelium. The present study aimed at evaluating the PDE4 activity and expression, the relation between the inflammation and cAMP-activity in the lungs, and potential interventions of PDE inhibitors and antiinflammatory drugs in the reduction of lung inflammation and goblet cell hyperplasia in allergic rats. The total leukocyte number and eosinophil number in bronchoalveolar lavage fluid and PDE4 activity and expression in lungs significantly increased in OVA-sensitized and challenged allergic rat. Lung histol. showed an increased infiltration of inflammatory cells in the perivascular and peribronchial spaces, structure changes and goblet cell hyperplasia in the OVA-sensitized and -challenged allergic rats. A significant correlation was observed between the increases in cAMP-PDE activity and inflammation in the lung. Those OVA-induced changes were prevented by pretreatment with PDE inhibitor in a dose-related patterns and with glucocorticosteroid. The authors found an increase in the proportion of PDE4 and PDE4 gene expression, while a decrease in the proportion of PDE3 in the lung of allergic rats. Incubation with different PDE inhibitors down-regulated OVA-induced cAMP hydrolysis. The data suggest that PDE4C may play an important role in the airway inflammation, remodeling and goblet cell hyperplasia after repeated challenge of sensitized rats.  
 REFERENCE COUNT: 38 THERE ARE 38 CITED REFERENCES AVAILABLE FOR THIS  
 RECORD. ALL CITATIONS AVAILABLE IN THE RE  
 FORMAT

L7 ANSWER 2 OF 9 CAPLUS COPYRIGHT 2007 ACS ON STN  
 ACCESSION NUMBER: 2006:967566 CAPLUS  
 DOCUMENT NUMBER: 145:369507  
 TITLE: Effects of ciclamilast, a new PDE4 inhibitor, on airway hyperresponsiveness, PDE4D expression and airway inflammation in a murine model of asthma  
 AUTHOR(S): Deng, Yang-mei; Xie, Qiang-min; Tang, Hui-fang; Sun, Jian-gang; Deng, Jun-fang; Chen, Ji-qiang; Yang, Shui-you  
 CORPORATE SOURCE: Zhejiang Respiratory Drugs Research Laboratory of State Food And Drug Administration, Medical Science College of Zhejiang University, Hangzhou, Peop. Rep. China  
 SOURCE: European Journal of Pharmacology (2006), 547(1-3), 125-135  
 CODEN: EJPHAZ; ISSN: 0014-2999  
 PUBLISHER: Elsevier B.V.  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English  
 AB PDE4 (phosphodiesterase-4) plays a critical role in pathogenesis of allergic asthma and chronic obstructive pulmonary disease (COPD). PDE4 inhibitors are presently under clin. development for the treatment of asthma and/or COPD. Ciclamilast, a new PDE4 inhibitor, is a piclamilast (RP 73401) structural analog, but has a more potent inhibitory effect on PDE4 and inflammation in the airway tissues and less side effects than that of piclamilast. In this study, we elucidate primarily on the roles of compound on PDE4 enzyme in physiol. and pathol. processes in a mouse model of asthma. The sensitized/challenged mice were reexposed to ovalbumin and airway response to inhaled methacholine was monitored. Orally administration of ciclamilast, in a dose-dependent manner, significantly inhibited changes in lung resistance and lung dynamic compliance, as well as upregulation of cAMP-PDE activity, increase of PDE4D mRNA expression, but not PDE4B from lung tissue in the murine model. In addition, the compound dose-dependently reduced mRNA expression of eotaxin, tumor necrosis factor (TNF)- $\alpha$  and interleukin (IL)-4, but slightly increased mRNA expression of interferon (IFN)- $\gamma$  from lung tissue. Further, levels of eotaxin, TNF- $\alpha$  and IL-4, and eosinophil and neutrophil accumulation in bronchoalveolar lavage fluid were also significantly reduced. Pathol. examination, goblet cell hyperplasia and inflammatory cells infiltration in lung tissue were suppressed by treatment with ciclamilast. A significant correlation was observed between the increases in PDE4D mRNA expression and airway hyperresponsiveness. These studies confirm that inhibitory effect of ciclamilast on airway hyperresponsiveness includes its inhibiting PDE4D mRNA expression, down-modulating PDE4 activity, anti-inflammation and anti-mucus hypersecretion, and ciclamilast may have therapeutic potential for the treatment of asthma.  
 REFERENCE COUNT: 59 THERE ARE 59 CITED REFERENCES AVAILABLE FOR THIS  
 RECORD. ALL CITATIONS AVAILABLE IN THE RE  
 FORMAT

L7 ANSWER 4 OF 9 CAPLUS COPYRIGHT 2007 ACS ON STN  
 ACCESSION NUMBER: 2004:353146 CAPLUS  
 DOCUMENT NUMBER: 140:375085  
 TITLE: Preparation of arylindenopyridines as phosphodiesterase inhibitors and adenosine A2a receptor antagonists  
 INVENTOR(S): Heintzelman, Geoffrey R.; Averill, Kristin M.; Dodd, John H.; Demarest, Keith T.; Tang, Yuting; Jackson, Paul F.  
 PATENT ASSIGNEE(S): Ortho-Muniel Pharmaceutical, Inc., USA  
 SOURCE: U.S. Pat. Appl. Publ., 136 pp., Cont.-in-part of U.S. Pat. Appl. 2003 212,089.  
 CODEN: USXXCO  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 5  
 PATENT INFORMATION:  

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2004082578	A1	20040429	US 2002-259139	20020927
US 6903109	B2	20050607		
US 2003212089	A1	20031113	US 2002-123389	20020416
US 6958328	B2	20051025		
US 2004127510	A1	20040701	US 2003-678562	20031003
US 2006154949	A1	20060713	US 2005-42281	20050124
US 2005239782	A1	20051027	US 2005-148114	20050608
US 2005239812	A1	20051027	US 2005-169549	20050629
US 2005239810	A1	20051027	US 2005-170044	20050629
US 2005267142	A1	20051201	US 2005-169554	20050629
US 2005267138	A1	20051201	US 2005-170484	20050629
US 2005267139	A1	20051201	US 2005-170569	20050629
US 2006009481	A1	20060112	US 2005-196154	20050803
US 2005277637	A1	20051215	US 2005-197612	20050804
US 2007155760	A1	20070705	US 2006-560637	20061116
PRIORITY APPLN. INFO.:			US 2001-284465P	P 20010418
			US 2002-123389	A2 20020416
			US 2002-259139	A2 20020927
			US 2003-678562	A3 20031003
			US 2005-42281	A3 20050124

 OTHER SOURCE(S): MARPAT 140:375085  
 G1



AB This invention provides novel arylindenopyridines (shown as I: variables



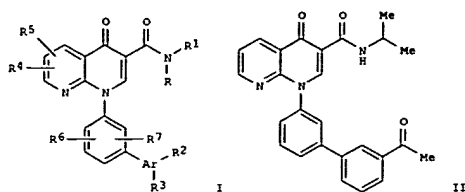
L7 ANSWER 4 OF 9 CAPLUS COPYRIGHT 2007 ACS ON STN (Continued)  
defined below and/or in claims: e.g.  
4-(3,5-dimethylphenyl)-2-methyl-5-oxo-  
5H-indeno[1,2-b]pyridine-3-carboxylic acid Me ester), and pharmaceutical  
comps. comprising same, useful for treating disorders ameliorated by  
antagonizing adenosine A2a receptors or by reducing phosphodiesterase (PDE)  
activity in appropriate cells. I are potent small mol. phosphodiesterase  
inhibitors that have demonstrated potency for inhibition of PDE7, PDE5, and PDE4; some I are potent small mol. PDE7  
inhibitors that have also demonstrated good selectivity against PDE5 and  
PDE4; data are provided for about 30 I. I are also antagonists of the  
adenosine A2a receptors that have demonstrated potency for the antagonism  
of adenosine A2a, A1, and A3 receptors; data are provided for about 45 I.  
This invention also provides therapeutic and prophylactic methods using  
the instant pharmaceutical comps. Although the methods of prepn. are  
not claimed, 23 example prepn. of intermediates and I are included; mass  
spectral data are tabulated for 284 examples of I. In I: R1 = COR5,  
COR6, CH, a lactone or lactam formed with R4, CONR7R8; R2 =  
H, (un)substituted alkyl, aryl, heteroaryl, heterocyclyl, cycloalkyl; R3 =  
H, halo, alkyl, arylalkyl, cycloalkyl, alkoxy, CN, carboalkoxy, CF3,  
alkylsulfonyl, NO2, OH, OCF3, carboxylate, aryl, heteroaryl,  
heterocyclyl;  
NR10R11; NR12COR13; R4 = H, alkyl, benzyl, NR13R14; X = S, O; R5, R6 = H,  
alkyl, aryl, arylalkyl; R7, R8 = H, alkyl, cycloalkyl, etc.; R10, R11 =  
H, alkyl, arylalkyl, etc.; R12, R14 = H, alkyl; R13 = H, alkyl, alkoxy, etc.  
REFERENCE COUNT: 85 THERE ARE 85 CITED REFERENCES AVAILABLE FOR  
THIS  
FORMAT RECORD. ALL CITATIONS AVAILABLE IN THE RE

L7 ANSWER 5 OF 9 CAPLUS COPYRIGHT 2007 ACS ON STN  
ACCESSION NUMBER: 2003:855799 CAPLUS  
DOCUMENT NUMBER: 139:350637  
TITLE: Preparation of 5-oxo and 5-thio derivatives of  
5H-indeno[1,2-b]pyridine with adenosine A2a receptor  
binding and phosphodiesterase inhibiting activity for  
the treatment of neurodegenerative disorders and  
inflammation related diseases  
INVENTOR(S): Heinzelman, Geoffrey R.; Averill, Kristin M.; Dodd,  
John H.; Demarest, Keith T.; Tang, Yuting; Jackson,  
Paul F.  
PATENT ASSIGNEE(S): Ortho-McNeil Pharmaceutical, Inc., USA  
SOURCE: PCT Int. Appl., 112 pp.  
CODEN: PIXXD2  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
FAMILY ACC. NUM. COUNT: 5  
PATENT INFORMATION:  
PATENT NO. KIND DATE APPLICATION NO. DATE  
WO 2003088963 A1 20031030 WO 2002-US30825 20020927  
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,  
CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,  
GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS,  
LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PH, PL,  
PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA,  
UG, UZ, VN, YU, ZA, ZM, ZW  
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,  
KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES,  
FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF,  
CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG  
US 2003212089 A1 20031113 US 2002-123389 20020416  
US 6958328 B2 20051025  
CA 2488929 A1 20031030 CA 2002-2488929 20020927  
AU 2002341875 A1 20031103 AU 2002-341875 20020927  
BR 2002015699 A 20050503 BR 2002-15699 20020927  
CN 1809349 A 20060726 CN 2002-810472 20020927  
MX 2004PA10307 A 20060222 MX 2004-PA10307 20041018  
IN 2005KN00303 A 20070928 IN 2005-KN303 20041116  
ZA 2005001390 A 20060830 ZA 2005-1390 20050216  
US 2002-123389 A 20020416  
OTHER SOURCE(S): MARPAT 139:350637  
GI  
\* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT \*

AB The title comps. (I: R1 = COR5 (wherein R5 = H, alkyl, aryl, arylalkyl),  
COR6 (R6 = H, alkyl, aryl, arylalkyl), CN, etc.; R2 = alkyl, aryl,  
heteroaryl, etc.; R3 = H, halo, alkyl, etc.; R4 = H, alkyl, CH2Ph, etc.;  
X = S, O), useful for treating disorders ameliorated by antagonizing  
adenosine A2a receptors or reducing PDE activity in

L7 ANSWER 5 OF 9 CAPLUS COPYRIGHT 2007 ACS ON STN (Continued)  
appropriate cells, were prepd. Thus, oxidn. of dihydropyridine II  
(prepn. given) afforded 81% III. The IC50 and inhibition data on PDE 4,5 and  
7A, and Ki on A2a and A1 receptors binding for representative comps. I were  
given. Pharmaceutical comps. comprising the compd. I are claimed. This  
invention also provides therapeutic and prophylactic methods using the  
instant pharmaceutical comps.  
REFERENCE COUNT: 31 THERE ARE 31 CITED REFERENCES AVAILABLE FOR  
THIS  
FORMAT RECORD. ALL CITATIONS AVAILABLE IN THE RE

L7 ANSWER 6 OF 9 CAPLUS COPYRIGHT 2007 ACS ON STN  
ACCESSION NUMBER: 2002:906219 CAPLUS  
DOCUMENT NUMBER: 138:4594  
TITLE: Preparation of 1-biaryl-[1,8]naphthyridin-4-one  
phosphodiesterase IV inhibitors for treatment of  
asthma and inflammation  
INVENTOR(S): Guay, Daniel; Girard, Mario; Hamel, Pierre;  
Laliberte, Sebastien; Priesen, Richard; Girard, Yves; Li, Chun  
PATENT ASSIGNEE(S): Merck Frosst Canada & Co., Can.  
SOURCE: PCT Int. Appl., 166 pp.  
CODEN: PIXXD2  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
FAMILY ACC. NUM. COUNT: 1  
PATENT INFORMATION:  
PATENT NO. KIND DATE APPLICATION NO. DATE  
WO 2002094823 A1 20021128 WO 2002-CA746 20020522  
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,  
CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,  
GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS,  
LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PH, PL,  
PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA,  
UG, US, UZ, VN, YU, ZA, ZM, ZW  
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH,  
CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR,  
BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG  
CA 2447765 A1 20021128 CA 2002-2447765 20020522  
AU 2002257459 A1 20021203 AU 2002-257459 20020522  
EP 1397359 A1 20040317 EP 2002-727127 20020522  
EP 1397359 B1 20050831  
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,  
IE, SI, LT, LV, FI, RO, MK, CY, AL, TR  
JP 2004534773 T 20041118 JP 2002-591496 20020522  
AT 303384 T 20050915 AT 2002-727127 20020522  
ES 2247325 T3 20060301 ES 2002-727127 20020522  
US 2003096829 A1 20030522 US 2002-154591 20020524  
US 6677351 B2 20040113  
PRIORITY APPLN. INFO.: US 2001-293247P P 20010524  
WO 2002-CA746 W 20020522  
OTHER SOURCE(S): MARPAT 138:4594  
GI



AB Title compds. I [wherein Ar = Ph, pyridyl, pyrimidyl, indolyl, quinolinyl, thienyl, pyridonyl, oxazolyl, oxadiazolyl, thiazolyl, imidazolyl, or heteroaryl oxides; R = H or alkyl; R1 = H or (un)substituted (cyclo)alkyl, alkoxy, alkenyl, alkynyl, heteroaryl, or heterocyclyl; R2 = H, halo, (cyclo)alkyl, alkoxy, amino, acyl, alkoxycarbonyl, alkylsulfamoyl, alkylsulfonyle, or (un)substituted Ph, heteroaryl, or heterocyclyl, etc.; R3 = H, OH, NH2, halo, (un)substituted alkyl; R4-R7 = independently H, halo, NH2, or (un)substituted alkyl or alkoxy; or pharmaceutically acceptable salts thereof] were prepared as phosphodiesterase IV (PDE4) inhibitors for the treatment of asthma and inflammation. For instance,

Et 3-(3-bromoanilino)-2-(2-chloronicotinoyl)acrylate was cyclized using NaH in THF and the resulting ester saponified to give 1-(3-bromophenyl)-1,4-dihydro-1,8-naphthyridin-4-one-3-carboxylic acid. Amidation with isopropylamine, followed by treatment with 3-acetylphenylboronic acid in the presence of trans-PdBr2(PPh3)2 and Na2CO3 in toluene and EtOH gave

II. I demonstrated PDE4 inhibitory activity by suppression of TNF- $\alpha$  secretion in LPS stimulated human blood with IC50 values generally ranging from 0.005  $\mu$ M to 15.4  $\mu$ M. In a SPA based PDE activity assay, I inhibited the hydrolysis of cAMP to AMP by human recombinant phosphodiesterase IVa with IC50 values between 34.3 nM and 134.0 nM.

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE

FORMAT

ACCESSION NUMBER: 2002:832790 CAPLUS

DOCUMENT NUMBER: 137:337793

TITLE: Preparation of arylindenopyridines as phosphodiesterase inhibitors  
Heintzelman, Geoffrey R.; Averill, Kristin M.; Dodd, John H.

INVENTOR(S):  
PATENT ASSIGNEE(S): Ortho-McNeil Pharmaceutical, Inc., USA

SOURCE: PCT Int. Appl., 91 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

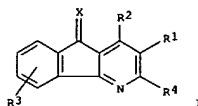
FAMILY ACC. NUM. COUNT: 5

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002085894	A1	20021031	WO 2002-US11823	20020416
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DO, EC, EE, ES, FI, GB, GD, GE, GM, GR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LA, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MY, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2445188	A1	20021031	CA 2002-2445188	20020416
AU 2002256225	A1	20021105	AU 2002-256225	20020416
EP 1385843	A1	20040204	EP 2002-725675	20020416
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
CN 1516698	A	20040728	CN 2002-811974	20020416
JP 2004532228	T	20041021	JP 2002-583421	20020416
PRIORITY APPLN. INFO.:			US 2001-284465P	20010418
			WO 2002-US11823	W 20020416

OTHER SOURCE(S): MARPAT 137:337793

GI



AB This invention provides novel arylindenopyridines (shown as I; variables defined below and/or in claims, e.g.  
4-(3,5-dimethylphenyl)-2-methyl-5-oxo-5H-indeno[1,2-b]pyridine-3-carboxylic acid Me ester), and pharmaceutical compns. comprising same, useful for treating disorders ameliorated by reducing phosphodiesterase (PDE) activity in appropriate cells. I are potent small mol. phosphodiesterase inhibitors that have demonstrated potency for inhibition of PDE7, PDE5, and PDE4;

some I are potent small mol. PDE7 inhibitors that have also demonstrated good selectivity against PDE5 and PDE4; data are provided for about 30 I. This invention also provides therapeutic and prophylactic methods using the instant pharmaceutical compns. Although the methods of prepn. are

not

claimed, 21 example prepn. of intermediates and I are included; mass spectral data are tabulated for 263 examples of I. In I: R1 is -COR5, COOR6, cyano, a lactone or lactam formed with R4, -CONR7R8. R2 is optionally substituted alkyl, aryl, heteroaryl, heterocyclyl and C3-7 cycloalkyl. R3 is 1-4 groups H, halo, C1-8 straight or branched chain alkyl, arylalkyl, C3-7 cycloalkyl, C1-8 alkoxy, cyano, C1-4 carboalkoxy, trifluoromethyl, C1-8 alkylsulfonyle, halogen, nitro, hydroxy, trifluoromethoxy, C1-8 carboxylate, aryl, heteroaryl, and heterocyclyl; -NR10R11; -NR12COR13. R4 is H, C1-3 straight or branched chain alkyl, benzyl and -NR13R14. X is S and O.

REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE

FORMAT

ACCESSION NUMBER: 2002:50304 CAPLUS

DOCUMENT NUMBER: 137:31970

TITLE: Differential effect of phosphodiesterase inhibitors on IL-13 release from peripheral blood mononuclear cells

AUTHOR(S): Yoshida, N.; Shimizu, Y.; Kitaichi, K.; Hiramatsu, K.; Takeuchi, M.; Tto, Y.; Kume, H.; Yamaki, K.; Suzuki, R.; Shibata, E.; Hasegawa, T.; Takagi, K.

CORPORATE SOURCE: Second Department of Internal Medicine and Laboratory Medicine, Nagoya University School of Medicine, Nagoya, 461-8673, Japan

SOURCE: Clinical and Experimental Immunology (2001), 126(3), 384-389

CODEN: CEXIAL; ISSN: 0009-9104

PUBLISHER: Blackwell Science Ltd.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Increased cAMP-phosphodiesterase (PDE) activity in peripheral blood leukocytes is associated with the immunol. inflammation that

characterizes allergic diseases, such as atopic dermatitis and allergic rhinitis. Recently, it has been found that IL-13 has similar biol. functions to IL-4. The aim here was to investigate the possible involvement of cAMP-PDE activity on IL-13 release from peripheral blood mononuclear cells (PBMC) from atopic asthma

patients. Phytohemagglutinin (PHA)-induced IL-13 release from PBMC was concentration-dependently inhibited by rolipram, a type 4 PDE inhibitor,

as well as by dibutyryl cAMP, a membrane-permeant cAMP analog. However, theophylline, a non-specific PDE inhibitor, and cilostazol, a type 3 PDE inhibitor, failed to inhibit IL-13 release. The inhibitory effect of rolipram was enhanced by the addition of forskolin (10-4 M), an adenylyl cyclase stimulator. PHA itself did not alter the intracellular cAMP level. Rolipram concentration-dependently increased cAMP level in

PHA-stimulated PBMC, and this increase was synergistically facilitated by the addition of

forskolin (10-4 M). Thus, type 4 PDE inhibitors, alone or synergistically in combination with forskolin, inhibit PHA-induced IL-13 release from

PBMC of atopic asthma patients by elevating intracellular cAMP concns. These inhibitors have the potential to exert an anti-inflammatory effect by inhibiting IL-13 production in allergic diseases such as atopic asthma.

REFERENCE COUNT: 41 THERE ARE 41 CITED REFERENCES AVAILABLE FOR THIS

RECORD. ALL CITATIONS AVAILABLE IN THE RE

FORMAT

L7 ANSWER 9 OF 9 CAPIUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2000-268097 CAPIUS

DOCUMENT NUMBER: 133:160077

TITLE: Beclomethasone decreases elevations in phosphodiesterase activity in human T lymphocytes  
AUTHOR(S): Crocker, I. Caroline; Church, Martin K.; Ohia, S. Edet; Townley, Robert G.

CORPORATE SOURCE: Division of Allergy, Creighton University, Omaha, NE, USA

SOURCE: International Archives of Allergy and Immunology (2000), 121(2), 151-160  
CODEN: IAAIEG; ISSN: 1018-2438

PUBLISHER: S. Karger AG

DOCUMENT TYPE: Journal

LANGUAGE: English

AB It has been reported that CD4+ T cells that have been activated in vivo or

in vitro contain elevated cAMP phosphodiesterase (PDE) activity. Since both PDE inhibitors and glucocorticoids have anti-inflammatory activity, the effect of beclomethasone on PDE activity was investigated. PDE activity was measured in CD4+ T cells after 24 h of culture with beclomethasone. The cells were obtained from the peripheral blood of nonatopic persons (nCells), preseasonal (pCells), seasonal (within the

1st

2 wk; sCells) and midseasonal (mCells) allergic rhinitics and asymptomatic allergic asthmatics (aCells). In addition, the effect of beclomethasone on Th2 cell lines and cells that had been activated in vitro with PHA or interleukin (IL)-2 was determined. PDE activity was decreased in a concentration-dependent manner by incubation of mCells, Th2 lines and PHA- or IL-2-activated CD4+ T cells with beclomethasone. However, beclomethasone did not modulate PDE activity in nCells, pCells, sCells, or aCells. Thus, beclomethasone decreases cAMP PDE activity in CD4+ T cells only when it has been increased by cell activation either in vitro or in vivo.

REFERENCE COUNT: 56 THERE ARE 56 CITED REFERENCES AVAILABLE FOR THIS

FORMAT RECORD. ALL CITATIONS AVAILABLE IN THE RE

=> FIL STNGUIDE  
COST IN U.S. DOLLARS

SINCE FILE	TOTAL
ENTRY	SESSION
54.52	54.73

FULL ESTIMATED COST

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)

SINCE FILE	TOTAL
ENTRY	SESSION
-8.58	-8.58

CA SUBSCRIBER PRICE

FILE 'STNGUIDE' ENTERED AT 11:37:53 ON 07 DEC 2007  
USE IS SUBJECT TO THE TERMS OF YOUR CUSTOMER AGREEMENT  
COPYRIGHT (C) 2007 AMERICAN CHEMICAL SOCIETY (ACS)

FILE CONTAINS CURRENT INFORMATION.  
LAST RELOADED: Nov 30, 2007 (20071130/UP).

=> d his

(FILE 'HOME' ENTERED AT 11:33:18 ON 07 DEC 2007)

FILE 'CAPLUS' ENTERED AT 11:33:35 ON 07 DEC 2007

L1	914 S PDE ACTIVITY
L2	0 S L1 AND FP ASSAY?
L3	75 S FP ASSAY?
L4	1 S L3 AND INFLAMMATORY?
L5	1 S L3 AND ALLERG?
L6	40 S L1 AND INFLAMMATORY?
L7	9 S L6 AND ALLERG?

FILE 'STNGUIDE' ENTERED AT 11:37:53 ON 07 DEC 2007

=> log y  
COST IN U.S. DOLLARS

SINCE FILE	TOTAL
ENTRY	SESSION
0.24	54.97

FULL ESTIMATED COST

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)

SINCE FILE	TOTAL
ENTRY	SESSION
0.00	-8.58

CA SUBSCRIBER PRICE

STN INTERNATIONAL LOGOFF AT 11:40:10 ON 07 DEC 2007